REMARKS

Claims 21 to 23 and 25 to 29 are pending in the present application, with claims 21 to 23 and 25 having been withdrawn from consideration as directed to non-elected subject matter. Claims 26 to 29 have been amended herein. Thus, upon entry of the present amendment, claims 26 to 29 will be under examination.

Regarding the amendments

Claims 26 and 27 have been amended to substitute the term "substantially pure" with the term "isolated." Support for substitution of "substantially pure" with "isolated" is provided both by teachings in the specification and by the art-accepted meanings of these terms. Further support for recitation of the term "isolated" can be found in the specification at page 55, lines 1-10, which indicates that an "isolated" PAMP polypeptide can be useful in a method of the invention. The specification supports recitation of the term "isolated" by teaching, for example, that a substantially pure molecule is substantially free from cellular components or other contaminants that are not the desired molecule (page 11, lines 9-13). Furthermore, the American Heritage Dictionary defines the word "isolate" as "to separate (a substance) in pure form from a combined mixture (The American Heritage® Dictionary of the English Language, Fourth Edition; Houghton Mifflin Company (2000))."

As set forth above, the amendment to claims 26 to 29 are supported by the specification and does not add new matter. Accordingly, Applicant respectfully requests that the Examiner enter the amendment.

Regarding the claim objection

The objection to claims 26 to 29 for reciting the term "substantially pure" is respectfully traversed. The Office Action asserts that the metes and bounds of the term "substantially pure" are unclear. Applicant respectfully submits that the metes and bounds of the term "substantially pure" would have been understood by those skilled in the art in view of teachings in the specification. In this regard, those skilled in the art would have recognized that a substantially pure molecule has been isolated from cellular components and contaminants other than the desired molecule (see, for example, page 11, lines 9-13). Nevertheless, to further prosecution, Applicant has substituted the objected term with the term "isolated." Therefore, Applicant requests that the Examiner withdraw the objection to claims 26 to 29.

Regarding the utility rejections under 35 U.S.C. § 101

The rejection of claims 26 to 29 under 35 U.S.C. § 101, as allegedly lacking utility is respectfully traversed. The Office Action alleges that the subject matter of the rejected claims lacks either a specific or well established utility.

In particular, the Office Action alleges (a) that detection of a PAMP polypeptide in the LNCaP cell line is not applicable to an *in vivo* diagnostic situation; (b) that it could not have been predicted that PAMP polypeptide SEQ ID NO:2 and variants exist in prostate tissue based on mRNA expression; (c) that proteins detected in prostate cancer patient sera, as described in the Declaration under Rule 132 submitted with Applicant's previous response, do not seem to include the 151 kDa PAMP polypeptide; and (d) that there is a lack of correlation between the claimed polypeptides and a known disease or disorder.

Applicant maintains that use of a PAMP polypeptide to generate antibodies reactive to PAMP is a specific, credible and substantial utility. Regarding the assertion in the Office Action that detection of a PAMP polypeptide in the LNCaP cell line cannot be applied to an *in vivo* diagnostic situation, Applicant submits herewith as Exhibit A a Declaration under Rule 132 by the inventor, Biaoyang Lin, which confirms teachings in the specification that an antibody generated using a PAMP polypeptide can be used to detect PAMP polypeptide expression *in vivo*. In his Declaration, Dr. Lin avers that an anti-PAMP monoclonal antibody designated 9E1-N1 was used to detect a PAMP polypeptide in cultured cells, serum samples and tissue samples. As set forth in the Declaration, the anti-PAMP antibody confirmed expression of a 151 kDa PAMP polypeptide in LNCaP cells and tissues such as ovary and testis (Figure 1, lane B; Figure 2). Furthermore, a 61 kDa PAMP polypeptide was detected in patient sera (Figure 1, lane D). Specificity of the anti-PAMP monoclonal was confirmed by pre-incubation with the PAMP polypeptide used to

generate the antibody prior to use in Western blotting (Figure 1, lanes A and C).

Regarding whether proteins detected in prostate cancer patient sera include a PAMP polypeptide, Applicant points to Dr. Lin's Declaration, which as indicated above, confirms that serum from prostate cancer patients indeed contains a PAMP polypeptide. As is shown in Figure 1, the 9E1-N1 monoclonal antibody detected the 61 kDa PAMP polypeptide contained in prostate cancer patient sera (lane D) and failed to detect the PAMP polypeptide in a control experiment in which the antibody was pre-incubated with the PAMP peptide used to generate the antibody (lane C).

As further evidence of the utility of a PAMP polypeptide, Applicant submits data corroborating that the PAMP polypeptide is differentially expressed in normal verses cancerous prostate tissue. Specifically, immunohistochemistry staining of normal and prostate cancer tissue sections is shown in Figure 3 of the attached Declaration. PAMP polypeptide expression was high in cancerous prostate tissue (Figure 3A and B) and low in normal prostate and adjacent tissue (Figure 3C). Dr. Lin's findings with patient serum samples further emphasized the usefulness of anti-PAMP antibodies as diagnostic reagents. As set forth in the attached Declaration, sera obtained from normal individuals and prostate cancer patients could be distinguished based on levels of PAMP polypeptide expression detected by the anti-PAMP monoclonal antibody (Figure 4), with high levels of PAMP expression observed in advanced prostate cancer patient sera, lower levels of PAMP expression observed in

early stage prostate cancer and undetectable levels of PAMP expression observed in normal sera. These results, which are summarized in Table 1, corroborate the utility of an anti-PAMP antibody as a marker for diagnosing prostate cancer.

Regarding a correlation between the claimed polypeptide and a known disease or disorder, Dr. Lin's Declaration confirms that a high level PAMP polypeptide expression, as detected either in prostate tissue or in serum, correlates with prostate cancer. These results further corroborate the use of a PAMP polypeptide in making anti-PAMP antibodies, as disclosed in the specification, as a specific, substantial and credible utility for the claimed PAMP polypeptides.

In view of the above remarks and accompanying Declaration by Dr. Lin, Applicant submits that the claimed invention satisfies the requirements for utility. It is therefore respectfully requested that the rejection of claims 26 to 29 under 35 U.S.C. § 101 be removed.

Regarding the rejection of claims 26 to 29 under 35 U.S.C. § 112, first paragraph, enablement

I. Utility

The objection to the specification and corresponding rejection of claim 26 to 29 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement on the ground that the claimed invention lacks utility are respectfully traversed.

Applicant submits that the specification provides enablement for the full scope of claims 26 to 29 by teaching a specific, substantial and credible utility of the claimed PAMP polypeptides. As is described above with respect to the rejection of claims 26 to 29 under 35 U.S.C. § 101, the specification teaches that the claimed PAMP polypeptides are useful, for example, for preparing an anti-PAMP antibody. Dr. Lin's Declaration corroborates the teachings in the specification regarding the utility of the claimed PAMP polypeptides by confirming that anti-PAMP antibodies can be used to detect PAMP polypeptides expressed in a variety of samples, including tissue samples and human sera. Furthermore, the Declaration indicates that anti-PAMP antibodies can be used in diagnostic applications for detecting prostate cancer.

In view of the above remarks and accompanying Declaration by Dr. Lin, it is submitted that the claimed invention satisfies the requirements for utility and, therefore, it is respectfully requested that the rejection of claims 26 to 29 under 35 U.S.C. § 112, first paragraph, be removed.

II. Claims 28 and 29

Regarding enablement of claims 28 and 29, the Office Action alleges that the specification lacks guidance regarding (a) which or how many original amino acids(s) of a PAMP polypeptide can be substituted; (b) which type of substitution of a PAMP polypeptide besides conservative substitution can be made,

and (c) which amino acids of a PAMP polypeptide can be deleted or inserted.

Applicant submits that the specification provides sufficient guidance to allow those skilled in the art to make and use the claimed PAMP polypeptides containing an amino acid sequence having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, and including residues 1075 to 1382 of SEQ ID NO: 2. In this regard, the specification provides guidance for making the claimed polypeptides, for example, by teaching how many amino acids(s) of SEQ ID NO:2 can be substituted. In particular, the specification teaches that at most 10% or 5%, respectively, of a stretch of 350 residues of SEQ ID NO: 2 can be substituted to obtain a PAMP polypeptide as recited in claim 28 or 29.

The specification further teaches a variety of amino acid substitutions, in addition to conservative substitutions, that can be included in a PAMP polypeptide of claim 28 or 29. For example, the specification teaches that a PAMP polypeptide of the invention can be a naturally occurring variant of human PAMP SEQ ID NO: 2, such as a species homolog, including a mammalian homolog such as a murine, bovine, or primate homolog or a non-mammalian homolog (page 20, lines 5-10). Those skilled in the art would have appreciated that such naturally occurring variants of SEQ ID NO:2 would contain a variety of amino acid differences yet retain a PAMP polypeptide function. In addition, by teaching that a PAMP polypeptide having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO:2 can be a

species homolog, the specification provides guidance to those skilled in the art regarding which amino acids of a PAMP polypeptide can be substituted, deleted or inserted. In this regard, those skilled in the art would have appreciated that amino acid residues conserved between SEQ ID NO:2 and a species homolog can be less tolerant of change, whereas amino acid residues that are not conserved can be more tolerant of change. Thus, because only routine methods would have been required, for example, to prepare a species homolog of SEQ ID NO:2 or another polypeptide having at least 90% or 95% amino acid identity with at least 350 residues of SEQ ID NO: 2, and including residues 1075 to 1382 of SEQ ID NO:2, undue experimentation would not have been required for one skilled in the art to make and use the PAMP polypeptides of claims 28 and 29.

In sum, Applicant submits that using guidance provided by the specification and routine molecular biology methods, one skilled in the art would have been able to make the PAMP polypeptides of claims 28 and 29 without undue experimentation. In view of the above remarks, Applicant respectfully requests that the Examiner reconsider and remove the enablement rejection under 35 U.S.C. § 112, first paragraph.

Regarding the rejection under 35 U.S.C. § 112, first paragraph, written description

The objection to the specification and corresponding rejection of claims 28 and 29 under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient description of the

claimed PAMP polypeptides to convey to one skilled in the art that Applicant had possession of the claimed invention prior to filing the application, are respectfully traversed.

Claims 28 and 29 stand rejected on the ground that the specification lacks description of PAMP polypeptides that are at least 90% or 95% identical to 350 amino acids of SEQ ID NO:2, including amino acids 1075 to 1382 of SEQ ID NO:2. Applicant submits that sufficient written description is provided to convey to one skilled in the art that the inventor had possession of the invention of claims 28 and 29 when the application was filed. The specification provides guidance, for example, by disclosing at least 350 residues of SEQ ID NO:2 (Figure 1) and by teaching nucleotide sequences that can be common to the PAMP polypeptides of claims 28 and 29. In particular, a PAMP polypeptide having 90% identity with 350 residues of SEQ ID NO:2, including residues 1075 to 1382 of SEQ ID NO:2, as recited in claim 28, contains only 1 out of 10 amino acids different from the specified amino acids of SEQ ID NO:2. Similarly, a PAMP polypeptide having 95% identity with of 350 residues of SEQ ID NO:2, including residues 1075 to 1382 of SEQ ID NO: 2, as recited in claim 28, contains only 1 in 20 amino acids different from the specified amino acids of SEQ ID NO:2. Given the written description of SEQ ID NO:2 in Figure 1 and the further disclosure in the specification, it would have been clear to the skilled person that Applicant was in possession of the claimed invention at the time the application was filed. In view of the above, Applicant respectfully requests that the Examiner reconsider and remove the written description rejection of claims 28 and 29 under 35 U.S.C. § 112.

CONCLUSION

In view of the amendments and the remarks submitted herein, Applicant submits that the claims are in condition for allowance and respectfully requests a notice to that effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell if there are any questions relating to this application.

Respectfully submitted,

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